A Note on Twin–Singleton Differences in Asthma

Simon Francis Thomsen,[1] Kirsten Ohm Kyvik,[2] and Vibeke Backer[1]

[1] *Department of Respiratory Medicine, Bispebjerg Hospital, Copenhagen, Denmark*
[2] *Institute of Regional Health Research Services and The Danish Twin Registry, Epidemiology, Institute of Public Health, University of Southern Denmark, Odense, Denmark*

Twins constitute a valuable resource for genetic studies of asthma. However, critics argue that twins are 'special' in terms of prenatal environment and upbringing and therefore nonrepresentative. In respect to asthma a small range of studies report differential morbidity in twins compared with singletons. We review some of the possible explanations for these findings and conclude that results from twin studies of asthma can be extrapolated to the general population.

Twins are on average born 3 weeks prior to term with a birthweight that is on average a 1000 g below that of singletons. Furthermore, twins experience more obstetric complications and cesarean sections than singletons (Kyvik, 2000). Immaturity has been associated with an increased risk of infant respiratory distress syndrome (IRDS; Brooks et al., 2001), which has been associated with an increased risk of childhood asthma (Smith et al., 2004). Moreover, cesarean sections have been shown to be a risk factor for asthma both in children and adults (Renz-Polster et al., 2005; Xu et al., 2001). Finally, the risk of various atopic outcomes like asthma, hay fever, and eczema is influenced by low birthweight (Katz et al., 2003; Nepomnyaschy & Reichman, 2006) although a protective effect of low birthweight has also been demonstrated (Bolte et al., 2004). In theory, these observations point to an increased risk of atopic morbidity in twins. However, results from twin studies of asthma seem not to support this view. The aim of this research note is to identify and review studies, which have specifically compared asthma prevalence rates in twins and singletons within the same sampling frame using the same methodology.

Method of Identification of Research Papers Used in This Review

We performed a search in Medline combining the words *twin, twin study, prevalence, incidence, occurrence, rate, and asthma*. Studies which reported on the prevalence of asthma in twins were identified. Related articles were identified and the reference list of each article was examined.

Prevalence and Admission Rates for Asthma

Räsänen and colleagues studied 3065 Finnish twin pairs and found that the heavier twin at birth (as indicated by ponderal index) had an increased risk of asthma at age 16 compared with his or her twin brother or sister (Räsänen at al., 2000). The relationship was stronger in fraternal than in identical twins consistent with common genetic influences on asthma and birthweight. Moreover, Canpolat et al. showed that the heavier twin at birth among birthweight discordant twins was more likely to develop IRDS (Canpolat et al., 2006). Others have supported this finding although results are conflicting (Hacking at al., 2001; Webb & Shaw, 2001). One twin study even suggested that the susceptibility to IRDS was primarily genetic in origin (van Sonderen et al., 2002). Thus, the relationship between birthweight and risk of asthma is still incompletely understood. In particular, it is not clear whether the increased risk of asthma observed at the extreme ends of the birthweight spectrum in singletons applies to the mode of foetal growth observed in multiples. In fact, low birthweight may in some instances be protective for asthma-related outcomes in twins, whereas extreme prematurity may lead to a hightened risk.

Strachan and colleagues observed that Scottish twins were half as likely as singletons to be admitted for asthma in early childhood (rate ratio = .47; Strachan et al., 2000). The authors concluded that twins in general had a reduced risk of atopic diseases compared with singletons. In particular, twin sibships were seen as special cases of large family size, which is a known protective factor for development of atopic disease (*hygiene hypothesis*; Strachan, 1989). Another observation in that study, however, was that twins were more likely than singletons to be admitted for acute bronchitis and bronchiolitis (rate ratio = 1.37). Bronchitis and bronchiolitis are fairly common in early childhood especially among subjects with

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Address for correspondence: Simon Francis Thomsen, Department of Respiratory Medicine, Bispebjerg Hospital, DK-2400 Copenhagen NV, Denmark. E-mail: sft@city.dk

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Table 1

Population-Based Studies of Asthma Prevalence in Twins

Study (1° author)	Country	Age group (Years)	Number (Pairs)	Prevalence[1] (%)	Diagnostic method
Harvald & Hauge (1956)	Denmark	46–86	1900	1.7	Physician diagnosed asthma
Skadhauge et al. (1999)	Denmark	12–41	11,688	6.0/6.5	Self-reported ever asthma
Edfors-Lubs (1971)	Sweden	46–85	6996	3.5/4.0	Self-reported ever asthma
Lichtenstein & Svartengren (1997)	Sweden	7–9	1480	8.0/4.0 18.0/10.0	Self-reported physician diagnosed or current asthma and self-reported ever wheezing or parent-report
Harris et al. (1997)	Norway	18–25	2570	6.0/5.4	Self-reported ever asthma
Nystad et al. (2005)[2]	Norway	18–35	3334	8.1	Self-reported ever asthma
Nieminen et al. (1991)	Finland	28–80	13,888	1.8/2.1	Record-linkage with hospital discharges, and reimbursed medications
Laitinen et al. (1998)	Finland	16	1713	4.7/3.1	Self-reported ever physician diagnosed asthma
Van Beijsterveldt & Boomsma (2007)	Netherlands	5	8633	10.2/7.2	Parent-reported ever physician diagnosed ever asthma
Koeppen-Schomerus et al. (2001)	England/Wales	4	4910	20.1/16.6	Ever had medication for asthma
Strachan et al. (2001)	England	18–72	873	/14.1	Self-reported ever asthma
Duffy et al. (1990)	Australia	18–88	3808	13.8/12.9	Self-reported ever asthma or wheezing
Clarke et al. (2000)	Australia	8–18	1262	24.7	Parent-reported current wheeze
Hallstrand et al. (2005)	United States	32[3]	1384	11.1/15.8	Self-reported ever physician diagnosed asthma

Note: [1]Estimates separated by a / denote prevalence for males and females, respectively

[2]Same population studied by Harris et al. (1997)

[3]Mean age

atopic heredity (Sigurs et al., 1995). Moreover, infant bronchiolitis is a significant predictor for asthma later in life (Sigurs et al., 2005). Asthma and bronchiolitis, especially when accompanied by wheezing, are possible indicators of the same vulnerable airway and may be difficult to tell apart in infants and small children (Martinez et al., 1995). The underrepresentation of twins among those admitted for asthma was consequently balanced by an overrepresentation of related diseases among twins, that is, the various diagnoses were possible indicators of the same underlying disorder. Moreover, admission of one twin to hospital could have led to recognition and prophylactic treatment of asthma in the co-twin (Strachan et al., 2000).

Multiple population-based studies of twins of various ages report prevalence rates of asthma (Table 1). Generally, these estimates seem not to deviate from figures obtained from studies of nontwin populations. In particular, results from the Danish, Australian, and Finnish twin registries suggest comparable rates in twins and singletons (Duffy et al., 1990; Huovinen & Kaprio, 2001; Skadhauge et al., 1999). However, lack of similar methods of ascertainment and diagnostics complicates comparison between studies.

A study by Bråbäck and Hedberg used similar methods to assess asthma prevalence in twins and singletons (Bråbäck & Hedberg, 1998); they observed a 17% reduced rate of asthma and a 27% reduced rate of allergic rhinitis in multiples compared to singletons among ~ 150.000 male army conscripts in Sweden. These findings could be due to prenatal events but were attributed mainly to breastfeeding patterns and exposure to cross-infections within twins.

Conclusions

Twins differ from singletons in respect to mode of delivery, birthweight, and neonatal respiratory morbidity. Moreover, there is some evidence that twins have a reduced rate of asthma in childhood (Strachan et al., 2000) and adolescence (Bråbäck & Hedberg, 1998). Causes for this may be due to differences in the above mentioned risk factors; alternative explanations include diagnostic misclassification or differences in healthcare seeking behavior of mothers of twins.

A multitude of population-based studies report prevalence rates of asthma in adult twins that are indistinguishable from rates observed in the general singleton population. These results are consistent with studies of other traits like for example mortality, adult cognitive abilities, and type I-diabetes that are all similar in twins and singletons (Christensen et al., 1995; Kyvik et al., 1995; Posthuma et al., 2000). However, we acknowledge that the conclusions of this review relies on only the few studies which have directly compared asthma prevalence rates in twins and singletons within the same sampling frame using the same methodology. To be able to draw more firm conclusions we therefore encourage that population-based studies are carried out with the aim to explicitly compare the prevalence of asthma in twins and singletons. We conclude that twins constitute a representative framework within which causes for asthma can be studied, and consequently that results from twin studies of asthma can be extrapolated to the general population.

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